



Original Article

The role of prostate MRI in clinical staging of prostate cancer before radical prostatectomy

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Keywords:

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Abstract

Objective: Transrectal ultrasonography (TRUS) guided biopsy is the main method used for the diagnosis of prostate cancer. However, it may be challenging to determine the extraprostatic extension (EPE) and seminal vesicle invasion (SVI) based solely on pathology alone. Newer imaging techniques may have the potential to improve differentiation between localized and locally advanced diseases. The objective of this study is to evaluate the accuracy of mpMRI in the determination of extraprostatic extension EPE and SVI of prostate cancer with regard to the final pathology, and to predict lymph node (LN) involvement.

Materials and Methods: This retrospective study evaluated the data from the medical records of male patients with prostate cancer who underwent preoperative mpMRI (at either 3.0 Tesla or 1.5 Tesla) followed by either robotic-assisted laparoscopic radical prostatectomy or laparoscopic radical prostatectomy, between January 2017 and October 2022. The area under the receiver operating characteristic curve (AUC) value was used in multivariable analysis to compare the performance of mpMRI and clinical data (prostate-specific antigen, ISUP category) in predicting pathologic EPE or SVI.

Results: The study looked at the data pertinent to 98 men with prostate cancer who underwent an MRI scan (mpMRI) before surgery (radical prostatectomy). The average age was 67 and the average PSA level was 19.81 ng/ml. The final pathology was reviewed to see if the cancer had spread outside the prostate (extracapsular extension, EPE) or into the SVI. These are signs of a more advanced cancer. At radical prostatectomy a total of 56 out of 98 (57.14%) patients had pathologic EPE, and 22 out of 98 (22.45%) patients had pathologic SVI. To determine the relationship between mpMRI staging and pathological staging, univariate analysis was conducted. EPE and SVI were combined to characterize them as locally progressed diseases and to enhance effective prediction. The data indicated 50.88%, 95.12%, 93.55%, and 58.21% of cases, for specificity, sensitivity, positive predictive value, and negative predictive value respectively. In summary, the mpMRI has a strong ability to inform the treatment of locally advanced disease due to its ability to determine the EPE and SVI on the final pathology. The limited level of sensitivity is currently limiting and warrants further research.

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Conclusion: This study suggests that mpMRI can be a valuable tool for the identification of prostate cancer in patients who are unlikely to have advanced stages of the disease (EPE or SVI). However, due to its limited sensitivity, it may limit the diagnosis of cases of advanced cancer. Therefore, a negative mpMRI result should not completely rule out the possibility of advanced disease, and additional evaluation may be necessary.

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Introduction

The most recent data indicates that prostate cancer is currently the fifth most frequent cancer in men in Thailand.¹ The incidence of prostate cancer has been declining during the previous few years.² and in the period 1993 to 2017, the age-adjusted death rate from prostate cancer has also steadily decreased. However, a more recent study has found that the death rate has remained constant in more recently.³

The diagnosis of prostate cancer typically involves a two-pronged approach: initial tests to see if further evaluation is needed, followed by a biopsy if the initial tests raise suspicion. The initial tests consist of a digital rectal examination (DRE) and measurement of prostate-specific antigen (PSA) levels. If the initial tests suggest a possibility of prostate cancer, a biopsy will likely be recommended. This biopsy is performed using a thin needle to extract a small sample of prostate tissue, often guided by transrectal ultrasonography (TRUS). Pathology reports are based on the Gleason scoring system for biopsied specimens. The clinical staging of prostate cancer is based on the TNM classification system from the AJCC Staging Manual, Eighth Edition.⁴

Treatment of prostate cancer patients is primarily guided by a risk stratification system, which includes clinical staging, Gleason grade, and PSA levels for the categorization of patients into risk groups.⁵ This allows for selection of the most appropriate treatment to effectively reduce the risk of recurrence and disease progression.

In recent years, multiparametric MRI (mpMRI) has significantly improved the processes of prostate cancer staging and characterization. For the most accurate diagnosis, a 3-Tesla MRI scanner is recommended for mpMRI. While lower magnetic field strengths (1.5-Tesla) can be used with additional equipment to enhance image quality⁶, mpMRI should not be considered a replacement for TRUS biopsy. It is not yet the gold

standard for the detection of prostate cancer itself.

Treatment decisions are heavily influenced by the distinction between organ-confined disease (T2) and extraprostatic disease (T3).⁷ The presence of extraprostatic extension (EPE) and seminal vesicle invasion (SVI) are accepted as accurate independent predictors of biochemical failure and metastasis.⁸

Any patient with prostate cancer who exhibits clinical signs of clinical localization may receive a radical prostatectomy (RP) as their initial course of treatment. Both robot-assisted laparoscopic radical prostatectomy (RALRP) and laparoscopic radical prostatectomy (LRP) are frequently performed and are believed to be comparable to conventional methods.⁹

The purpose of this study is to investigate whether mpMRI can result in the ability to distinguish between organ-confined (T2) and extraprostatic (T3) prostate cancer based on the final pathology, and to assess the potential for lymph node involvement. The objective of this study is to assess the ability for pre-operative mpMRI to predict EPE and SVI in the final prostatic specimen, and to assess potential lymph node involvement.

Materials and Methods

Study design

Retrospective diagnostic study.

Ethical approval given by the Ethics Committee Chiang Mai University (Study Code: SUR-2564-08177)

Population

Data was retrieved from the medical records of patients at Maharaj Nakorn Chiang Mai Hospital between January 2017 and October 2022. Informed consent was not obtained due to the retrospective nature of the study.

Inclusion criteria

- Male patients aged ≥ 45 years old.
- Had undergone RP due to prostate cancer.

- Underwent mpMRI prior to radical prostatectomy.

Exclusion criteria

- Has a pathological diagnosis of locally advanced disease or metastatic disease.
- Underwent external beam radiation therapy before undergoing radical prostatectomy.

Sample size

Formula used for calculation as described by Daniel, 1999 using data from a previous study: Sensitivity = 0.81, 1-Sensitivity = 0.19, Prevalence = 0.37, $d^2 = 0.08^2 = 0.0064$

$$n_{Se} = \frac{Z_{\frac{\alpha}{2}}^2 Se(1 - Se)}{d^2 \times Prev}$$

Calculated sample size = 127.38 = 128 patients

Study protocol

Patients who have been diagnosed with prostate cancer via TRUS biopsy based on abnormal DRE or high PSA levels are offered either a CT scan of the abdomen and pelvis or the mpMRI of the prostate for imaging investigations. If imaging shows no signs of locally advanced or metastatic disease, patients will be offered treatment options for prostate cancer. Patients choosing RP are advised further on surgical technique choices.

All patients undergo a pelvic phased-array 3-Tesla or 1.5-Tesla mpMRI using an endorectal coil (ERC). Three standard imaging sequences are used during mpMRI exams: T2-weighted imaging

(TWI), diffusion-weighted imaging (DWI), and dynamic contrast enhancement imaging (DCE). MRI-derived prostate volume (PV) is calculated using the ellipsoid formula: $0.52 \times (D1 \times D2 \times D3)$.¹⁰ Results are then reported based on PI-RADS grading criteria.¹¹ Current practice is for two radiologists to independently identify and report the presence of EPE and SVI based on the mpMRI.

The preoperative variables are recorded as follows: age, underlying medical condition, serum PSA level, symptoms at presentation, prostate volume measured by mpMRI, date of mpMRI, mpMRI PI-RADS score, and biopsy Gleason grade group according to the ISUP classification.

The postoperative variables are recorded as follows: final specimen pathological stage and ISUP grade group, types of surgical technique used, and number of days between mpMRI and RP (Fig. 1).

Data analysis

Using a Fisher's two-tailed exact test, the categorical data have been presented as frequency and percentage. Using a Mann-Whitney U test the mean and standard deviation of the continuous variables have been reported.

Sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and area under the receiver operating characteristic curve (AuROC) calculations were performed. Data analysis was done using STATA version 16.0.

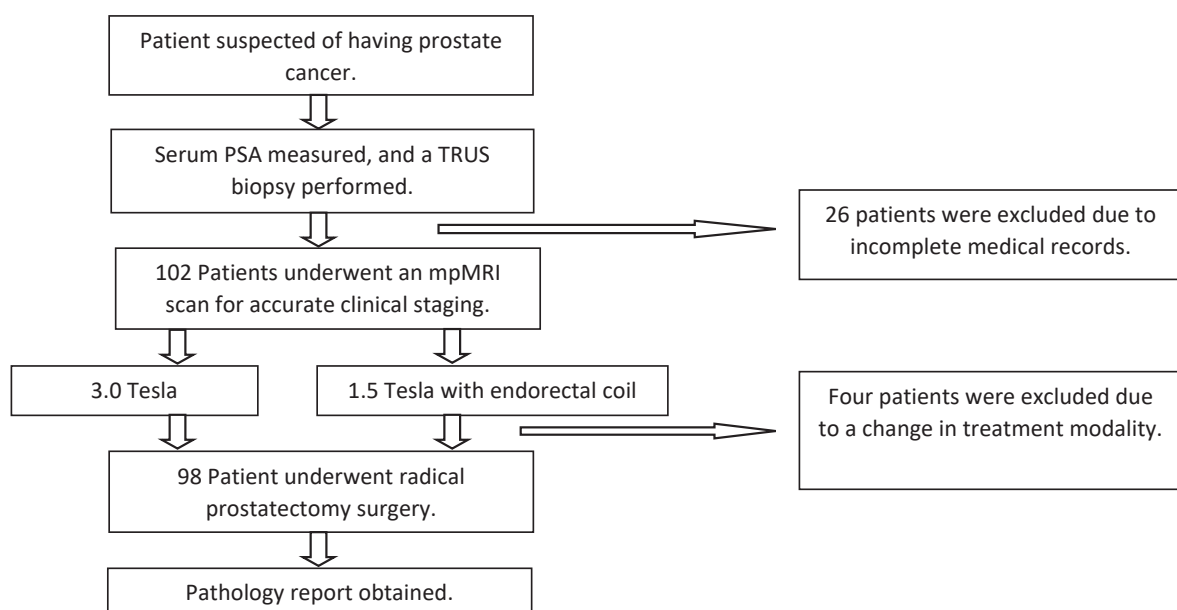


Figure 1. Study design diagram

Results

The study included data on 128 patients in total. Due to inadequate data records, patient had received other local treatments, a salvage RP performed, and not undergoing mpMRI before surgery, 30 patients were removed. 98 patients in all had data gathered for analysis.

Baseline characteristics of patients are shown in Table 1.

98 patients in all met the criteria for selection. Table 1 includes the demographics and clinical data. The mean age was 66.69 years old. The mean PSA was 19.81 ng/ml. Most prostate biopsies, 43 patients, were classified as ISUP category 2 (43.88%), followed by 22 patients classified as category 5 (22.45%), 15 patients classified as category 3 (15.31%), and 9 patients classified equally as categories 1 and 4 (18.36%). In the table, patient characteristics are displayed. In the preoperative imaging, the mpMRI enabled the identification of 31 patients with EPE (31.63%), and 13 patients with SVI (13.26%). In the RP samples, EPE was detected in 56 patients overall (57.14%), whereas SVI was detected in 22 patients (22.45%).

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the mpMRI in the identification of EPE or SVI are shown in Table 2.

The sensitivity, specificity, positive predictive value, and negative predictive value of the mpMRI in the detection of lymph node metastatic status is shown in Table 3.

The ROC curve for the detection of EPE or SVI using mpMRI are shown in Figure 2.

The ROC curve for the detection of lymph node metastatic status using mpMRI is shown in Figure 3.

Our analysis showed a statistically significant correlation ($p < 0.05$) between mpMRI staging and the final pathological staging of prostate cancer. In other words, mpMRI results compared well to the findings from tissue examination after surgery. The breakdown of mpMRI performance is as follows:

- **EPE and SVI Detection:** mpMRI demonstrated a high specificity (95.12%) for the identification of EPE or SVI suggesting the use of mpMRI is highly effective in correctly ruling out these conditions (low false positive rate). However, the sensitivity was moderate (50.88%), indicating mpMRI may miss some cases of EPE/

SVI (false negative rate). Overall accuracy for EPE/SVI detection was 69.39%.

- **Lymph Node Prediction:** mpMRI showed as being a very promising technique for the prediction of lymph node involvement with very high specificity (97.50%) suggesting mpMRI is highly effective in identifying patients in whom there is no lymph node involvement. However, the sensitivity was lower (38.89%), suggesting the use of mpMRI may miss some patients with positive lymph nodes. The overall accuracy for lymph node prediction was 86.73%.

Discussion

RP is the current gold standard treatment for localized prostate cancer, offering similar oncological outcomes to external beam radiotherapy.¹² However, this surgery can cause side effects, specifically erectile dysfunction (up to 74.70%) and urine incontinence (up to 21.30%) within a year of the procedure.¹³

Current clinical staging and diagnosis of prostate cancer primarily rely on PSA levels and DRE. However, these methods have limitations in comparison with mpMRI with regard to detecting whether the disease has spread beyond the prostate gland.¹⁴ Additionally, mpMRI also more effective than a pelvis and abdominal CT scan in terms of the detection of EPE.¹⁵ As a result, it has been suggested that mpMRI be used as a technique to determine whether there is locally advanced disease before the actual surgery.

This study evaluated the ability of the use of mpMRI to predict EPE and SVI, as well as lymph node involvement, in patients diagnosed with prostate cancer in whom RP was being considered. Patients underwent mpMRI scans prior to surgery, and their mpMRI results were compared to the final pathology after RP.

This study found high mpMRI specificity (95.12%) for the identification of the presence of EPE or SVI confirmed by final pathology. This suggests that mpMRI can help reduce unnecessary exclusions from curative treatments by minimizing false-positive results. However, the sensitivity for EPE/SVI detection was moderate (50.88%). These results are in alignment with other studies, for example a study by Jeong et al reported moderate sensitivity for EPE (43.00%) and SVI (34.90%) but high specificity for both (84.20% and 93.80%, respectively).^{16,17} These

Table 1. Baseline characteristics data of prostate cancer patients (N=98)

Parameters	n (%) [Range]
Underlying disease	
Hypertension	46 (46.94)
Dyslipidemia	29 (29.59)
Diabetes mellitus	17 (17.35)
Kidney disease	6 (6.12)
Heart disease	12 (12.24)
Symptoms at presentation	
Gross hematuria	2 (2.04)
Lower urinary tract symptoms	65 (66.33)
No symptoms	32 (32.65)
Prostate-specific antigen (ng/ml)	19.82 (21.03) [4.58-154.00]
Prostate volume at MRI (ml)	39.83 (20.19) [14.6-135.00]
Time period between MRI and radical prostatectomy (days)	132.75 (157.41) [5-1,127]
Surgical modality	
Laparoscopic radical prostatectomy	33 (33.67)
Robot-assisted laparoscopic radical prostatectomy	65 (66.33)
ISUP category and Gleason score on prostate biopsy	
1 (3+3)	9 (9.18)
2 (3+4)	43 (43.88)
3 (4+3)	15 (15.31)
4 (4+4, 3+5, 5+3)	9 (9.18)
5 (4+5, 5+4, 5+5)	22 (22.45)
Extraprostatic extension cases from mpMRI	31 (31.63)
Seminal vesicle invasion cases from mpMRI	13 (13.26)
Pathologic extraprostatic extension cases	56 (57.14)
Pathologic seminal vesicle invasion cases	22 (22.45)
mpMRI modality	
1.5 Tesla with endorectal coil	27 (27.55)
3.0 Tesla	71 (72.44)
MRI PIRADS	
3	10 (10.20)
4	33 (33.67)
5	55 (56.12)
Surgical margin	
Negative	42 (42.86)
Positive	56 (57.14)
Perineural invasion	
Negative	18 (18.37)
Positive	80 (81.63)
Lymphovascular invasion	
Negative	61 (62.24)
Positive	37 (37.76)
Lymph node(s)	
Negative	80 (81.63)
Positive	18 (18.37)
Tumor%*, Mean (SD)	37.25 (25.28) [5-100]

SD = standard deviation

*Percentage of prostate involved in the tumor

Table 2. Diagnostic accuracy of mpMRI in the identification of extraprostatic extension (EPE) or seminal vesicle invasion (SVI)

Parameters	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Surgical modality				
LRP	35.71	89.47	71.43	65.38
RALRP	55.81	100.00	100.00	53.66
ISUP category and Gleason score on radical prostatectomy				
1 (3+3)	-	-	-	88.89
2 (3+4)	45.45	90.48	83.33	83.33
3 (4+3)	50.00	100.00	100.00	50.00
4 (4+4, 3+5, 5+3)	50.00	100.00	100.00	71.43
5 (4+5, 5+4, 5+5)	60.00	100.00	100.00	20.00
mpMRI modality				
1.5 Tesla with endorectal coil	27.78	100.00	100.00	40.91
3.0 Tesla	61.54	93.75	92.31	66.67
MRI PIRADS				
3	33.33	100.00	100.00	77.78
4	23.53	87.50	66.67	51.85
5	64.86	100.00	100.00	58.06
Surgical margin				
Negative	27.27	93.55	60.00	78.38
Positive	56.52	100.00	100.00	33.33
Perineural invasion				
Negative	50.00	93.75	50.00	93.75
Positive	50.91	96.00	96.55	47.06
Lymphovascular invasion				
Negative	42.31	94.29	84.62	68.75
Positive	58.06	100.00	100.00	31.58
Lymph node (s)				
Negative	55.81	94.59	92.31	64.81
Positive	35.71	100.00	100.00	30.77

PPV = positive predictive value, NPV = negative predictive value, LRP = laparoscopic radical prostatectomy, RALRP = robot-assisted laparoscopic radical prostatectomy

findings collectively highlight that mpMRI alone may not be sufficient for definitive local staging of prostate cancer.

However, mpMRI offers significant advantages as a non-invasive diagnostic tool. It does not require hospitalization or antibiotic prophylaxis, unlike some procedures. This study also showed that both 1.5-Tesla and 3.0-Tesla MRI scanners with ERC achieved similar accuracy and specificity in the detection of EPE/SVI and lymph node involvement. However, the sensitivity was lower in the case of the 1.5-Tesla scanner in comparison to the 3.0-Tesla scanner.

The limited sensitivity of mpMRI for the detection of EPE or SVI can be attributed to several factors. These include host factors such as prostate inflammation or recent biopsy, as well as the

limitations of the technique itself. For instance, mpMRI may be unclear with the identification of the periprostatic fat plane or when the seminal vesicle plane is obliterated.¹⁸

While mpMRI shows promise in the other areas of prostate cancer diagnosis, its accuracy with regard to the prediction of lymph node involvement remains under investigation. Some studies suggest the procedure has potential, but more research is needed. However, the established strengths of the use of mpMRI in the detection of EPE and SVI can still benefit prostate cancer patients. By accurately identifying these factors, mpMRI can help select patients who are more likely to benefit from pelvic lymph node dissection during RP, potentially improving patient selection for this procedure.

Table 3. Diagnostic accuracy of mpMRI in the detection of lymph node metastatic status

Parameters	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Surgical modality				
LRP	-	-	-	96.67
RALRP	41.18	95.83	77.78	82.14
ISUP category and Gleason score on radical prostatectomy				
1(3+3)	-	-	-	88.89
2(3+4)	-	-	-	90.70
3(4+3)	50.00	90.91	66.67	83.33
4(4+4, 3+5, 5+3)	-	-	-	88.89
5(4+5, 5+4, 5+5)	62.50	92.86	83.33	81.25
mpMRI modality				
≥ 1.5 Tesla with endorectal coil	50.00	100.00	100.00	87.50
≥ 3.0 Tesla	96.61	96.61	66.67	87.69
MRI PIRADS				
≥ 3	-	-	-	-
≥ 4	50.00	96.55	66.67	93.33
≥ 5	35.71	97.56	83.33	81.63
Surgical margin				
Negative	0	97.50	-	95.12
Positive	43.75	97.50	87.50	81.25
Perineural invasion				
Negative	-	-	-	94.44
Positive	41.18	96.83	77.78	85.92
Lymphovascular invasion				
Negative	0	98.18	0	90.00
Positive	58.33	96.00	87.50	82.76
Lymph node (s)				
Negative	-	97.50	-	-
Positive	-	61.11	-	-

PPV = positive predictive value, NPV = negative predictive value, LRP = laparoscopic radical prostatectomy, RALRP = robot-assisted laparoscopic radical prostatectomy

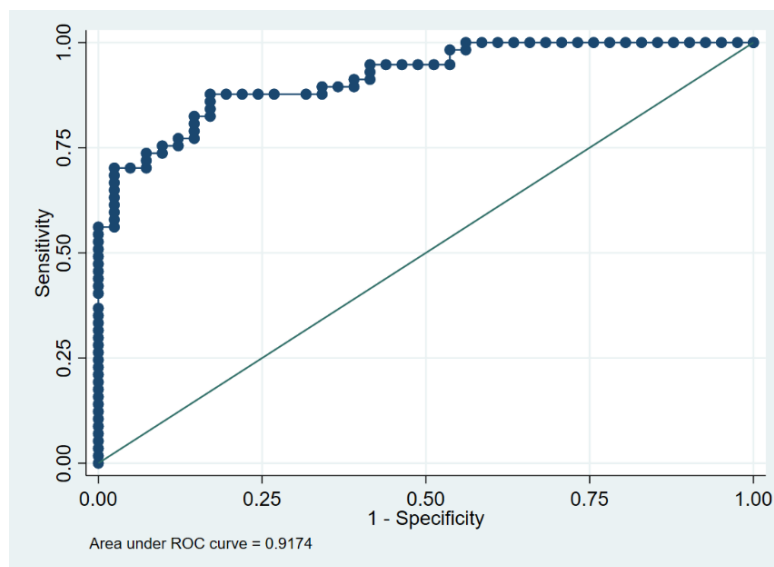


Figure 2. ROC curve for detection of EPE or SVI by mpMRI
Area Under Receiver Operating Characteristic curve (AuROC) = 0.9174

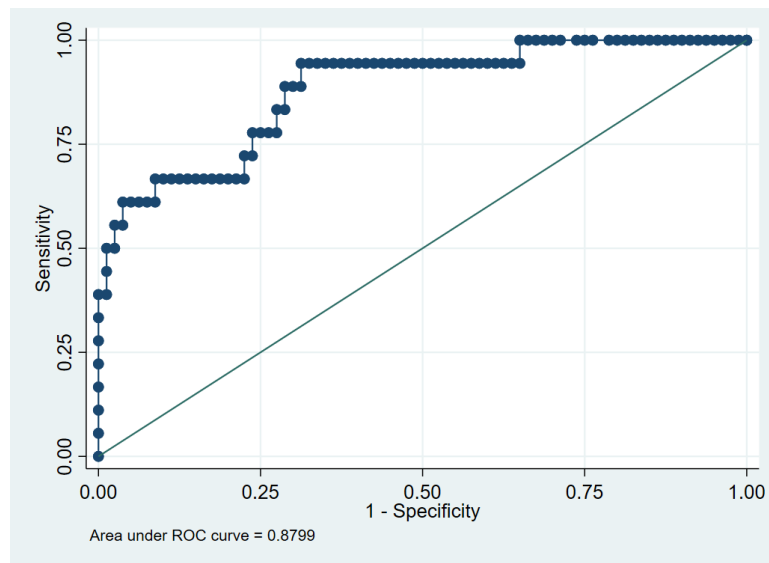


Figure 3. ROC curve for detection of lymph node metastatic status
Area Under Receiver Operating Characteristic curve (AuROC) = 0.8799

This study has both strengths and limitations. While its retrospective nature is a drawback, a key strength is that the radiologists evaluated all images prior to surgery, eliminating the possibility of selection bias. However, due to the non-uniform use of mpMRI, we were unable to determine the time interval between biopsy and mpMRI for all patients. This is important because the average time between mpMRI and surgery in this study was quite extended at 132 days, which could be a relevant factor in influencing disease progression and potentially affecting the pathological staging of cancer.

Conclusion

mpMRI is a promising tool for prostate cancer diagnosis, particularly with regard to the identification of EPE/SVI and potentially reducing unnecessary exclusions from curative treatments. However, the limitations surrounding its sensitivity necessitate further research, especially with regard to predictions pertinent to lymph node involvement. Future studies are warranted and should aim for a more uniform time interval between mpMRI and surgery to minimize potential confounding factors.

Conflict of Interest

The authors declare no conflict of interest.

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